Hybridization Chain Reaction in LSPR based biosensing for the detection of microRNAs

Andrea Miti (1), Sophie Thamm (3), Philipp Müller (3), Andrea Csáki (3), Wolfgang Fritzsche (3), Giampaolo Zuccheri (1,2)

(1) Department of Pharmacy and Biotechnology, University of Bologna, Italy.
(2) S3 Center, Institute of Nanoscience of the Italian CNR.
(3) Institute of Photonic Technology, Albert-Einstein-Str. 9, 07745 Jena, Germany

Hybridization Chain Reaction is a completely isothermal and Enzyme-free self assembling reaction involing a few species of hairpin-like DNA strands in solution. These hairpins are able to trigger the formation of long double stranded DNA nanostrutures when a specific sequence is present (1). HCR can be employed as amplification strategy in DNA based biosensing to reach higher sensitivity and specificity. In the past years we implementd HCR for the specific detection of pathogenic DNA testing the suitability with electrochemical and SPR transduction (2). MicroRNAs are attracting great attention as new powerful biomarkers: they are short non coding RNAs with regulatory roles, involved in many cellular process such as proliferation, differentiation, apoptosis and metabolsim in general. They are found to be deregulated in many pathological phenomena such as infections and tumors, and their concentration can give information about the status of the disease. Since common lab-based techniques often have difficulties to get a fast, specific and sensitive detection of microRNAs, there is the need for alternative approaches. We worked on the design and the implementation of different HCR-based strategies for the specific detection of miRNAs through different transduction methods. Beside the implementation for electrochmical detection, we are now working on the adaptation for Localized Surface Plasmon Resonance sensing. The binding of the analyte on the surface of metallic nanoparticles can be detected monitoring the shift in the LSPR peak due to a change in the refractive index (3) (Fig. 2). The increase of the local amount of DNA given by HCR could be detected as well, leading to the amplification of the signal. No examples exploring HCR on LSPR based sensing are present in literature. Here we present a strategy based on HCR in which one of the hairpin is immobilized on gold nanoparticles, as a probe, for the detection of microRNAs (Fig1,2).

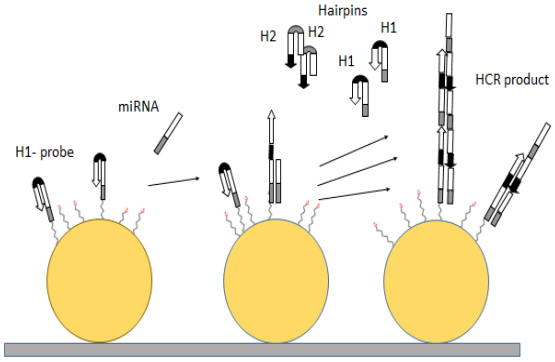

Fig. 1: Scheme of the miRNA detection through HCR on immobilized gold nanoparticles.

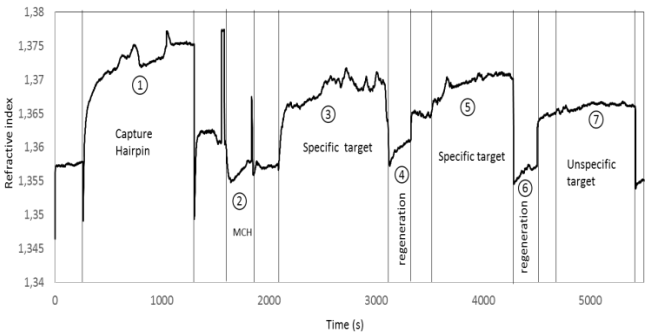

Fig. 2: Preliminary LSPR measurements showing probe immobilization (1) target hybridization (3 and 5) and interaction with unspecific sequence (7).

*[1] Dirks, R.M. and N.A. Pierce. PNAS, 2004. **101**(43): p. 15275-15278*
[2] Spiga, F.M. et al. Biosensors and Bioelectronics54(2014)102–108
[3] a) Jatschka J. et al. Sensing and Bio-Sensing Research. 7 (2016) 62-70. b) Joshi G. K. et al, Nano Lett. 14, (2014), 6955- 6963.